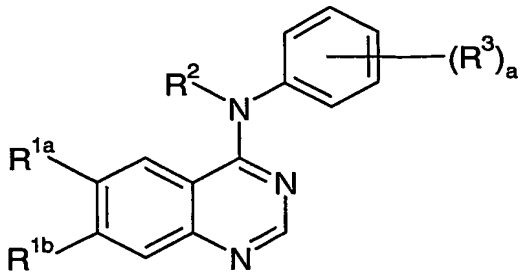
CLAIMS

1. A quinazoline derivative of the Formula I:



I

wherein:

one of R^{1a} or R^{1b} is a group of sub-formula (i)

$$Q^2\text{-}X^1\text{-}Z\text{-}Q^1\text{-}X^2\text{-}O\text{-}$$

(i)

where X^2 and X^1 are independently selected from a direct bond or a group $-[CR^4R^5]_m$, wherein m is an integer from 1 to 6,

Z is C(O), SO_2, $-C(O)NR^{10}$-, $-N(R^{10})C(O)$-, -C(O)O- or –OC(O)- where R^{10} is hydrogen or (1-6C)alkyl,

and each of R^4 and R^5 is independently selected from hydrogen, hydroxy, (1-4C)alkyl, halo(1-4C)alkyl, hydroxy (1-4C)alkyl, (1-4C)alkoxy(1-4C)alkyl, or R^4 and R^5 together with the carbon atom(s) to which they are attached form a (3-7)cycloalkyl ring, provided that when a group R^4 or R^5 is hydroxy, m is at least 2 and the carbon atom to which the hydroxy group is attached is not also attached to another oxygen or a nitrogen atom;

$\mathbf{Q^1}$ is (3-7C)cycloalkylene or heterocyclyl group, which is optionally substituted by one or two substituents selected from halogeno, trifluoromethyl, trifluoromethoxy, cyano, nitro, hydroxy, amino, carboxy, carbamoyl, acryloyl, (1-6C)alkyl, (2-8C)alkenyl, (2-8C)alkynyl, (1-6C)alkoxy, (2-6C)alkenyloxy, (2-6C)alkynyloxy, (1-6C)alkylthio, (2-6C)alkenylthio, (2-6C)alkynylthio, (1-6C)alkylsulfinyl, (2-6C)alkenylsulfinyl, (2-6C)alkynylsulfinyl, (1-6C)alkylsulfonyl, (2-6C)alkenylsulfonyl, (2-6C)alkynylsulfonyl, (1-6C)alkylamino, di-[(1-6C)alkyl]amino, (1-6C)alkoxycarbonyl, N-(1-6C)alkylcarbamoyl, N,N-di-[(1-6C)alkyl]carbamoyl, (2-6C)alkanoyl, (2-6C)alkanoyloxy, (2-6C)alkanoylamino,

N-(1-6C)alkyl-(2-6C)alkanoylamino, sulfamoyl, N-(1-6C)alkylsulfamoyl, N,N-di-[(1-6C)alkyl]sulfamoyl, (1-6C)alkanesulfonylamino, N-(1-6C)alkyl-(1-6C)alkanesulfonylamino, carbamoyl(1-6C)alkyl, N-(1-6C)alkylcarbamoyl(1-6C)alkyl, N,N-di-[(1-6C)alkyl]carbamoyl(1-6C)alkyl, sulfamoyl(1-6C)alkyl, N-(1-6C)alkylsulfamoyl(1-6C)alkyl, N,N-di-[(1-6C)alkyl]sulfamoyl(1-6C)alkyl, (2-6C)alkanoyl(1-6C)alkyl, (2-6C)alkanoyloxy(1-6C)alkyl, (2-6C)alkanoylamino(1-6C)alkyl, N-(1-6C)alkyl-(2-6C)alkanoylamino(1-6C)alkyl and (1-6C)alkoxycarbonyl(1-6C)alkyl;

Q^2 is an aryl or heteroaryl group, said aryl or heteroaryl group being optionally substituted by one of more substituents selected from halogeno, trifluoromethyl, trifluoromethoxy, cyano, nitro, hydroxy, amino, carboxy, carbamoyl, acryloyl, (1-6C)alkyl, (2-8C)alkenyl, (2-8C)alkynyl, (1-6C)alkoxy, (2-6C)alkenyloxy, (2-6C)alkynyloxy, (1-6C)alkylthio, (2-6C)alkenylthio, (2-6C)alkynylthio, (1-6C)alkylsulfinyl, (2-6C)alkenylsulfinyl, (2-6C)alkynylsulfinyl, (1-6C)alkylsulfonyl, (2-6C)alkenylsulfonyl, (2-6C)alkynylsulfonyl, (1-6C)alkylamino, di-[(1-6C)alkyl]amino, (1-6C)alkoxycarbonyl, N-(1-6C)alkylcarbamoyl, N,N-di-[(1-6C)alkyl]carbamoyl, (2-6C)alkanoyl, (2-6C)alkanoyloxy, (2-6C)alkanoylamino, N-(1-6C)alkyl-(2-6C)alkanoylamino, sulfamoyl, N-(1-6C)alkylsulfamoyl, N,N-di-[(1-6C)alkyl]sulfamoyl, (1-6C)alkanesulfonylamino, N-(1-6C)alkyl-(1-6C)alkanesulfonylamino, carbamoyl(1-6C)alkyl, N-(1-6C)alkylcarbamoyl(1-6C)alkyl, N,N-di-[(1-6C)alkyl]carbamoyl(1-6C)alkyl, sulfamoyl(1-6C)alkyl, N-(1-6C)alkylsulfamoyl(1-6C)alkyl, N,N-di-[(1-6C)alkyl]sulfamoyl(1-6C)alkyl, (2-6C)alkanoyl(1-6C)alkyl, (2-6C)alkanoyloxy(1-6C)alkyl, (2-6C)alkanoylamino(1-6C)alkyl, N-(1-6C)alkyl-(2-6C)alkanoylamino(1-6C)alkyl and (1-6C)alkoxycarbonyl(1-6C)alkyl,

and wherein any (1-6C)alkyl, (2-8C)alkenyl, (2-8C)alkynyl and (2-6C)alkanoyl substituent on Q^1 or Q^2 optionally bears one or more substituents (for example 1, 2 or 3) which may be the same or different selected from halogeno, hydroxy and (1-6C)alkyl and/or optionally a substituent selected from cyano, nitro, carboxy, (2-8C)alkenyl, (2-8C)alkynyl, (1-6C)alkoxy, hydroxy(1-6C)alkoxy, (1-4C)alkoxy(1-6C)alkoxy, (2-6C)alkanoyl, (2-6C)alkanoyloxy and NR^aR^b, wherein R^a is hydrogen or (1-4C)alkyl and R^b is hydrogen or (1-4C)alkyl, and wherein any (1-4C)alkyl in R^a or R^b optionally bears one or more substituents (for example 1, 2 or 3) which may be the same or different selected from halogeno and hydroxy and/or optionally a substituent selected from cyano, nitro,

(2-4C)alkenyl, (2-4C)alkynyl, (1-4C)alkoxy, hydroxy(1-4C)alkoxy and (1-2C)alkoxy(1-4C)alkoxy,

or R^a and R^b together with the nitrogen atom to which they are attached form a 4, 5 or 6 membered ring, which optionally bears 1 or 2 substituents, which may be the same or different, on an available ring carbon atom selected from halogeno, hydroxy, (1-4C)alkyl and (1-3C)alkylenedioxy , and may optionally bear on any available ring nitrogen a substituent (provided the ring is not thereby quaternised) selected from (1-4C)alkyl, (2-4C)alkanoyl and (1-4C)alkylsulfonyl,

and wherein any (1-4C)alkyl or (2-4C)alkanoyl group present as a substituent on the ring formed by R^a and R^b together with the nitrogen atom to which they are attached, optionally bears one or more substituents (for example 1, 2 or 3) which may be the same or different selected from halogeno and hydroxy and/or optionally a substituent selected from (1-4C)alkyl and (1-4C)alkoxy;

and wherein any heterocyclyl group Q^1- group optionally bears 1 or 2 oxo (=O) or thioxo (=S) substituents;

and the other of R^{1a} or R^{1b} is a group R^1 which is selected from hydrogen, hydroxy, (1-6C)alkoxy, (2-6C)alkenyloxy, (2-6C)alkynyloxy, or a group of the formula :

$$Q^4-X^3-$$

wherein X^3 is a direct bond or is selected from O or S, and Q^4 is (3-7C)cycloalkyl, (3-7C)cycloalkyl-(1-6C)alkyl, (3-7C)cycloalkenyl, (3-7C)cycloalkenyl-(1-6C)alkyl, heterocyclyl or heterocyclyl-(1-6C)alkyl,

and wherein adjacent carbon atoms in any (2-6C)alkylene chain within a R^1 substituent are optionally separated by the insertion into the chain of a group selected from O, S, SO, SO_2, $N(R^4)$, CO, $CH(OR^4)$, $CON(R^4)$, $N(R^4)CO$, $SO_2N(R^4)$, $N(R^4)SO_2$, CH=CH and C≡C wherein R^4 is hydrogen or (1-6C)alkyl,

and wherein any CH_2=CH- or HC≡C- group within a R^1 substituent optionally bears at the terminal CH_2= or HC≡ position a substituent selected from halogeno, carboxy, carbamoyl, (1-6C)alkoxycarbonyl, N-(1-6C)alkylcarbamoyl, N,N-di-[(1-6C)alkyl]carbamoyl, amino-(1-6C)alkyl, (1-6C)alkylamino-(1-6C)alkyl and di-[(1-6C)alkyl]amino-(1-6C)alkyl or from a group of the formula :

$$Q^5-X^4-$$

wherein X^4 is a direct bond or is selected from CO and $N(R^5)CO$, wherein R^5 is hydrogen or (1-6C)alkyl, and Q^5 is heterocyclyl or heterocyclyl-(1-6C)alkyl,

and wherein any alkyl or alkylene group within a R^1 substituent optionally bears one or more halogeno, (1-6C)alkyl, hydroxy, cyano, amino, carboxy, carbamoyl, sulfamoyl, (1-6C)alkoxy, (1-6C)alkylthio, (1-6C)alkylsulfinyl, (1-6C)alkylsulfonyl, (1-6C)alkylamino, di-[(1-6C)alkyl]amino, (1-6C)alkoxycarbonyl, N-(1-6C)alkylcarbamoyl, N,N-di-[(1-6C)alkyl]carbamoyl, (2-6C)alkanoyl, (2-6C)alkanoyloxy, (2-6C)alkanoylamino, N-(1-6C)alkyl-(2-6C)alkanoylamino, N-(1-6C)alkylsulfamoyl, N,N-di-[(1-6C)alkyl]sulfamoyl, (1-6C)alkanesulfonylamino and N-(1-6C)alkyl-(1-6C)alkanesulfonylamino, or from a group of the formula:

$$-X^5-Q^6$$

wherein X^5 is a direct bond or is selected from O, S, SO, SO_2, $N(R^6)$, CO, $CH(OR^6)$, $CON(R^6)$, $N(R^6)CO$, $SO_2N(R^6)$, $N(R^6)SO_2$, $C(R^6)_2O$, $C(R^6)_2S$ and $C(R^6)_2N(R^6)$, wherein R^6 is hydrogen or (1-6C)alkyl, and Q^6 is (3-7C)cycloalkyl, (3-7C)cycloalkyl-(1-6C)alkyl, (3-7C)cycloalkenyl, (3-7C)cycloalkenyl-(1-6C)alkyl, heterocyclyl or heterocyclyl-(1-6C)alkyl,

and wherein any heterocyclyl group within a substituent on R^1 optionally bears 1, 2 or 3 substituents, which may be the same or different, selected from halogeno, trifluoromethyl, cyano, nitro, hydroxy, amino, carboxy, carbamoyl, formyl, mercapto, (1-6C)alkyl, (2-8C)alkenyl, (2-8C)alkynyl, (1-6C)alkoxy, (2-6C)alkenyloxy, (2-6C)alkynyloxy, (1-6C)alkylthio, (1-6C)alkylsulfinyl, (1-6C)alkylsulfonyl, (1-6C)alkylamino, di-[(1-6C)alkyl]amino, (1-6C)alkoxycarbonyl, N-(1-6C)alkylcarbamoyl, N,N-di-[(1-6C)alkyl]carbamoyl, (2-6C)alkanoyl, (2-6C)alkanoyloxy, (2-6C)alkanoylamino, N-(1-6C)alkyl-(2-6C)alkanoylamino, N-(1-6C)alkylsulfamoyl, N,N-di-[(1-6C)alkyl]sulfamoyl, (1-6C)alkanesulfonylamino, and N-(1-6C)alkyl-(1-6C)alkanesulfonylamino, or from a group of the formula:

$$-X^6-R^7$$

wherein X^6 is a direct bond or is selected from O, $N(R^8)$ and C(O), wherein R^8 is hydrogen or (1-6C)alkyl, and R^7 is halogeno-(1-6C)alkyl, hydroxy-(1-6C)alkyl, carboxy-(1-6C)alkyl, (1-6C)alkoxy-(1-6C)alkyl, cyano-(1-6C)alkyl, amino-(1-6C)alkyl, (1-6C)alkylamino-(1-6C)alkyl, di-[(1-6C)alkyl]amino-(1-6C)alkyl, (2-6C)alkanoylamino-(1-6C)alkyl, (1-6C)alkoxycarbonylamino-(1-6C)alkyl, carbamoyl-(1-6C)alkyl, N-(1-6C)alkylcarbamoyl-(1-6C)alkyl, N,N-di-[(1-6C)alkyl]carbamoyl-(1-6C)alkyl, (2-6C)alkanoyl-(1-6C)alkyl or (1-6C)alkoxycarbonyl-(1-6C)alkyl,

and wherein any heterocyclyl group within a substituent on R^1 optionally bears 1 or 2 oxo or thioxo substituents;

R^2 is selected from hydrogen and (1-6C)alkyl;

each R^3, which may be the same or different, is selected from halogeno, cyano, nitro, hydroxy, amino, carboxy, carbamoyl, sulfamoyl, trifluoromethyl, (1-6C)alkyl, (2-8C)alkenyl, (2-8C)alkynyl, (1-6C)alkoxy, (2-6C)alkenyloxy, (2-6C)alkynyloxy, (1-6C)alkylthio, (1-6C)alkylsulfinyl, (1-6C)alkylsulfonyl, (1-6C)alkylamino, di-[(1-6C)alkyl]amino, (1-6C)alkoxycarbonyl, N-(1-6C)alkylcarbamoyl, N,N-di-[(1-6C)alkyl]carbamoyl, N-(1-6C)alkylsulfamoyl, and N,N-di-[(1-6C)alkyl]sulfamoyl

a is 1, 2, 3, 4 or 5;

or a pharmaceutically acceptable salt thereof;

subject to the following provisos:

(i) when Q^2 is aryl, then R^{1a} is a group of sub-formula (i) defined above and R^{1b} is the group R^1 defined above; and

(ii) the compound of formula I is not one of the following:

N-(3,4-dichlorophenyl)-7-[({4-[(3,5-dimethylisoxazol-4-yl)carbonyl]morpholin-2-yl}methyl)oxy]-6-(methyloxy)quinazolin-4-amine;

N-(3,4-dichlorophenyl)-7-({[4-(furan-3-ylcarbonyl)morpholin-2-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine;

7-[({4-[(2-chloropyridin-3-yl)carbonyl]morpholin-2-yl}methyl)oxy]-N-(3,4-dichlorophenyl)-6-(methyloxy)quinazolin-4-amine; or

7-[({4-[(6-chloropyridin-3-yl)carbonyl]morpholin-2-yl}methyl)oxy]-N-(3,4-dichlorophenyl)-6-(methyloxy)quinazolin-4-amine.

2. A quinazoline derivative according to any one of the preceding claims wherein X^2 is a direct bond.

3. A quinazoline derivative according to claim 1 or claim 2, wherein R^{1a} is a group of sub-formula (i), and R^{1b} is a group R^1 as defined in claim 1.

4. A quinazoline derivative according to claim 1 or claim 2, wherein R^{1a} is a group R^1, and R^{1b} is a group of sub-formula (i) as defined in claim 1.

5. A quinazoline derivative according to any one of the preceding claims, wherein R^1 is selected from hydrogen, hydroxy, (1-6C)alkoxy, (2-6C)alkenyloxy, (2-6C)alkynyloxy, or a group of the formula :

$$Q^4-X^3-$$

wherein X^3 is a direct bond or is O or S (particularly a direct bond or O), and Q^4 is (3-7C)cycloalkyl, (3-7C)cycloalkyl-(1-6C)alkyl, (3-7C)cycloalkenyl, (3-7C)cycloalkenyl-(1-6C)alkyl, heterocyclyl or heterocyclyl-(1-6C)alkyl, and wherein any alkyl or alkylene group within a R^1 substituent optionally bears one or more halogeno, (1-6C)alkyl, hydroxy, cyano, amino, carboxy, carbamoyl, sulfamoyl, (1-6C)alkoxy, (1-6C)alkylthio, (1-6C)alkylsulfinyl, (1-6C)alkylsulfonyl, (1-6C)alkylamino, di-[(1-6C)alkyl]amino, (1-6C)alkoxycarbonyl, N-(1-6C)alkylcarbamoyl, N,N-di-[(1-6C)alkyl]carbamoyl, (2-6C)alkanoyl, (2-6C)alkanoyloxy, (2-6C)alkanoylamino, N-(1-6C)alkyl-(2-6C)alkanoylamino, N-(1-6C)alkylsulfamoyl, N,N-di-[(1-6C)alkyl]sulfamoyl, (1-6C)alkanesulfonylamino and N-(1-6C)alkyl-(1-6C)alkanesulfonylamino.

6. A quinazoline derivative according to claim 5 wherein R^1 is hydrogen, (1-6C)alkoxy and (1-4C)alkoxy(1-6C)alkoxy, and wherein any (1-6C)alkoxy group within R^1 optionally bears 1, 2 or 3 substituents, which may be the same or different, selected from hydroxy, fluoro and chloro.

7. A quinazoline derivative according to claim 6 wherein R^1 is selected from methoxy, ethoxy, isopropyloxy, cyclopropylmethoxy, 2-hydroxyethoxy, 2-fluoroethoxy, 2-methoxyethoxy, 2,2-difluoroethoxy, 2,2,2-trifluoroethoxy or 3-hydroxy-3-methylbutoxy.

8. A quinazoline derivative according to claim 5 wherein R^1 is methoxy.

9. A quinazoline derivative according to any one of the preceding claims wherein X^1 is suitably a direct bond or a (1-6C)alkylene group.

10. A quinazoline derivative according to claim 9 wherein X^1 is a direct bond or methylene or ethylene group.

11. A quinazoline derivative according to any one of the preceding claims wherein Z is selected from -C(O)-, -NR^{10}-C(O)- (wherein R^{10} is H or (1-6C)alkyl), and –O-C(O)-.

12. A quinazoline derivative according to claim 11, wherein Z is -C(O)-.

13. A quinazoline derivative according to claim 11, wherein Z is selected from -NH-C(O)- and –O-C(O)-.

14. A quinazoline derivative according to any one of the preceding claims wherein Q^1 is a non-aromatic saturated or partially saturated 3 to 10 membered monocyclic heterocyclic ring with up to five heteroatoms selected from oxygen, nitrogen and sulfur (but not containing any O-O, O-S or S-S bonds), and linked via a ring carbon atom, or a ring nitrogen atom (provided the ring is not thereby quaternised).

15. A quinazoline derivative according to any one of the preceding claims wherein Q^1 is selected from oxiranyl, oxetanyl, azetidinyl, tetrahydrofuranyl, tetrahydropyranyl, oxepanyl, oxazepanyl, pyrrolinyl, pyrrolidinyl, morpholinyl, tetrahydro-1,4-thiazinyl, 1,1-dioxotetrahydro-1,4-thiazinyl, piperidinyl, homopiperidinyl, piperazinyl, homopiperazinyl, dihydropyridinyl, tetrahydropyridinyl, dihydropyrimidinyl, tetrahydropyrimidinyl, tetrahydrothienyl, tetrahydrothiopyranyl, thiomorpholinyl, more specifically including for example, tetrahydrofuran-3-yl, tetrahydrofuran-2-yl-, tetrahydropyran-4-yl, tetrahydrothien-3-yl, tetrahydrothiopyran-4-yl, pyrrolidin-3-yl, pyrrolidin-2-yl, 3-pyrrolin-3yl-, morpholino, 1,1-dioxotetrahydro-4H-1,4-thiazin-4-yl, piperidino, piperidin-4-yl, piperidin-3-yl, piperidin-2-yl, homopiperidin-3-yl, homopiperidin-4-yl, piperazin-1-yl, 1,4-oxazepanyl, or 1,2,3,6-tetrahydropyridin-4-yl.

16. A quinazoline derivative according to any one of claims 11 to 16, wherein the group Q^2-X^1-Z- is linked to a nitrogen atom on a heterocyclic atom of Q^1.

17. A quinazoline derivative according to any one of the preceding claims, wherein Q^2 is a heteroaryl group, said heteroaryl group being optionally substituted by one of more substituents selected from halogeno, trifluoromethyl, trifluoromethoxy, cyano, nitro, hydroxy, amino, carboxy, carbamoyl, acryloyl, (1-6C)alkyl, (2-8C)alkenyl, (2-8C)alkynyl, (1-6C)alkoxy, (2-6C)alkenyloxy, (2-6C)alkynyloxy, (1-6C)alkylthio, (2-6C)alkenylthio, (2-6C)alkynylthio, (1-6C)alkylsulfinyl, (2-6C)alkenylsulfinyl, (2-6C)alkynylsulfinyl, (1-6C)alkylsulfonyl, (2-6C)alkenylsulfonyl, (2-6C)alkynylsulfonyl, (1-6C)alkylamino, di-[(1-6C)alkyl]amino, (1-6C)alkoxycarbonyl, N-(1-6C)alkylcarbamoyl, N,N-di-[(1-6C)alkyl]carbamoyl, (2-6C)alkanoyl, (2-6C)alkanoyloxy, (2-6C)alkanoylamino, N-(1-6C)alkyl-(2-6C)alkanoylamino, sulfamoyl, N-(1-6C)alkylsulfamoyl, N,N-di-[(1-6C)alkyl]sulfamoyl, (1-6C)alkanesulfonylamino, N-(1-6C)alkyl-(1-6C)alkanesulfonylamino, carbamoyl(1-6C)alkyl, N-(1-6C)alkylcarbamoyl(1-6C)alkyl, N,N-di-[(1-6C)alkyl]carbamoyl(1-6C)alkyl, sulfamoyl(1-6C)alkyl, N-(1-6C)alkylsulfamoyl(1-6C)alkyl, N,N-di-[(1-6C)alkyl]sulfamoyl(1-6C)alkyl, (2-6C)alkanoyl(1-6C)alkyl, (2-6C)alkanoyloxy(1-6C)alkyl, (2-6C)alkanoylamino(1-6C)alkyl, N-(1-6C)alkyl-(2-6C)alkanoylamino(1-6C)alkyl and (1-6C)alkoxycarbonyl(1-6C)alkyl,

and wherein any (1-6C)alkyl, (2-8C)alkenyl, (2-8C)alkynyl and (2-6C)alkanoyl substituent on Q^2 optionally bears one or more substituents (for example 1, 2 or 3) which may be the same or different selected from halogeno, hydroxy and (1-6C)alkyl and/or optionally a substituent selected from cyano, nitro, carboxy, (2-8C)alkenyl, (2-8C)alkynyl, (1-6C)alkoxy, hydroxy(1-6C)alkoxy, (1-4C)alkoxy(1-6C)alkoxy, (2-6C)alkanoyl, (2-6C)alkanoyloxy and NR^aR^b, wherein R^a is hydrogen or (1-4C)alkyl and R^b is hydrogen or (1-4C)alkyl, and wherein any (1-4C)alkyl in R^a or R^b optionally bears one or more substituents (for example 1, 2 or 3) which may be the same or different selected from halogeno and hydroxy and/or optionally a substituent selected from cyano, nitro, (2-4C)alkenyl, (2-4C)alkynyl, (1-4C)alkoxy, hydroxy(1-4C)alkoxy and (1-2C)alkoxy(1-4C)alkoxy,

or R^a and R^b together with the nitrogen atom to which they are attached form a 4, 5 or 6 membered ring, which optionally bears 1 or 2 substituents, which may be the same or different, on an available ring carbon atom selected from halogeno, hydroxy, (1-4C)alkyl and (1-3C)alkylenedioxy , and may optionally bear on any available ring nitrogen a substituent (provided the ring is not thereby quaternised) selected from (1-4C)alkyl, (2-4C)alkanoyl and (1-4C)alkylsulfonyl,

and wherein any (1-4C)alkyl or (2-4C)alkanoyl group present as a substituent on the ring formed by R^a and R^b together with the nitrogen atom to which they are attached, optionally bears one or more substituents (for example 1, 2 or 3) which may be the same or different selected from halogeno and hydroxy and/or optionally a substituent selected from (1-4C)alkyl and (1-4C)alkoxy.

18. A quinazoline derivative according to any one of the preceding claims, wherein Q^2 is a 5 or 6 membered heteroaryl ring which optionally contains one or more heteroatoms selected from oxygen, nitrogen or sulphur.

19. A quinazoline derivative according to claim 18 wherein Q^2 is selected from furyl, thienyl, pyrrolyl, pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, 1,2,3-triazolyl, 1,2,4-triazolyl, oxadiazolyl, furazanyl, thiadiazolyl or tetrazolyl.

20. A quinazoline derivative according to any one of claims 1 to 17, wherein Q^2 is a 9 or 10 membered bicyclic heteroaryl ring system which optionally contains one or more heteroatoms selected from oxygen, nitrogen or sulphur.

21. A quinazoline derivative according to claim 20, wherein Q^2 is selected from quinolinyl, isoquinolinyl, cinnolinyl, quinazolinyl, phthalazinyl, quinoxalinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzothiazolyl or purinyl.

22. A quinazoline derivative according to any one of claims 1 to 16, wherein Q^2 is an aryl group selected from phenyl and naphthyl.

23. A quinazoline derivative according to any one of the preceding claims wherein Q^2 optionally bears 1 or 2 substituents, which may be the same or different, selected from halogeno, hydroxy, nitro, amino, cyano, carbamoyl, (1-4C)alkyl, (1-4C)alkoxy, (2-4C)alkanoyl and (1-4C)alkylsulfonyl, (1-4C)alkylamino, di[(1-4C)alkyl]amino, *N*-[(1-4C)alkyl]carbamoyl, and *N,N*-di[(1-4C)alkyl]carbamoyl.

and wherein any (1-4C)alkyl, or (2-4C)alkanoyl group within Q^2 optionally bears 1 or 2 substituents, which may be the same or different, selected from halogeno, hydroxy and (1-6C)alkyl and/or optionally a substituent selected from cyano, (2-8C)alkenyl,

(2-8C)alkynyl, (1-6C)alkoxy, (2-6C)alkanoyl, (2-6C)alkanoyloxy and NR^aR^b, wherein R^a is hydrogen or (1-4C)alkyl and R^b is hydrogen or (1-4C)alkyl, and wherein any (1-4C)alkyl in R^a or R^b optionally bears one or more substituents (for example 1, 2 or 3) which may be the same or different selected from halogeno and hydroxy and/or optionally a substituent selected from cyano, and (1-4C)alkoxy,

or R^a and R^b together with the nitrogen atom to which they are attached form a 4, 5 or 6 membered ring which does not contain oxygen, which ring optionally bears 1 or 2 substituents, which may be the same or different, on an available ring carbon atom selected from halogeno, hydroxy, (1-4C)alkyl and (1-3C)alkylenedioxy, and may optionally bear on any available ring nitrogen a substituent (provided the ring is not thereby quaternised) selected from (1-4C)alkyl, (2-4C)alkanoyl and (1-4C)alkylsulfonyl,

and wherein any (1-4C)alkyl or (2-4C)alkanoyl group present as a substituent on the ring formed by R^a and R^b together with the nitrogen atom to which they are attached optionally bears one or more substituents (for example 1, 2 or 3), which may be the same or different, selected from halogeno and hydroxy and/or optionally a substituent selected from (1-4C)alkyl and (1-4C)alkoxy.

24. A quinazoline derivative according to claim 23 wherein Q^2 is optionally substituted by one or two groups, which may be the same or different, selected from halogeno, hydroxy, nitro, amino, cyano, carbamoyl, (1-4C)alkyl, (1-4C)alkoxy, (2-4C)alkanoyl and (1-4C)alkylsulfonyl, [(1-4C)alkyl]amino, di[(1-4C)alkyl]amino, *N*-[(1-4C)alkyl]carbamoyl, and *N,N*-di[(1-4C)alkyl]carbamoyl.

and wherein any (2-4C)alkanoyl group in a substituent on Q^2 optionally bears one or two substituents, which may be the same or different, selected from hydroxy and (1-3C)alkyl,

and wherein any (1-4C)alkyl group in a substituent on Q^2 optionally bears one or two substituents, which may be the same or different, selected from hydroxy, (1-4C)alkoxy and halogeno (particularly chloro and more particularly fluoro).

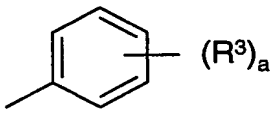
25. A quinazoline derivative according to claim 23 or claim 24 wherein Q^2 is unsubstituted or substituted by a (1-4C)alkyl group, a (1-4C)alkoxy group, halogeno, amino, nitro, cyano, carbamoyl, di-[(1-4C)alkyl]amino, and *N,N*-di[(1-4C)alkyl]carbamoyl.

26. A quinazoline derivative according to any one of the preceding claims wherein R^2 is hydrogen.

27. A quinazoline derivative according to any one of the preceding claims wherein a is 1, 2 or 3.

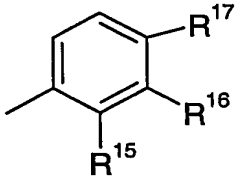
28. A quinazoline derivative according to any one of the preceding claims, wherein an R^3 is in the para position on the anilino ring, and this is selected from halogeno, cyano, nitro, hydroxy, amino, trifluoromethyl, (1-6C)alkyl, (2-8C)alkenyl, (2-8C)alkynyl, (1-6C)alkoxy, (2-6C)alkenyloxy, (2-6C)alkynyloxy, (1-6C)alkylthio, (1-6C)alkylamino and di-[(1-6C)alkyl]amino.

29. A quinazoline derivative according to any one of the preceding claims wherein the group of sub-formula (ii)



(ii)

in formula (I) is a group of sub-formula (iii)



(iii)

where one of R^{15} or R^{17} is hydrogen and the other is halogeno, and R^{16} is halogeno.

30. A quinazoline derivative according to claim 29 wherein the group of sub-formula (iii) is 3-chloro-2-fluorophenyl, or 3-chloro-4-fluorophenyl.

31. A compound selected from one of the following:

(1) *N*-(3-chloro-2-fluorophenyl)-6-{[1-(isoxazol-5-ylcarbonyl)piperidin-4-yl]oxy}-7-methoxyquinazolin-4-amine;

(2) *N*-(3-chloro-2-fluorophenyl)-7-methoxy-6-({1-[(3-methylisoxazol-5-yl)acetyl]piperidin-4-yl}oxy)quinazolin-4-amine;

(3) *N*-(3-chloro-2-fluorophenyl)-7-methoxy-6-({1-[(3-methylisoxazol-5-yl)carbonyl]piperidin-4-yl}oxy)quinazolin-4-amine;

(4) *N*-(3-chloro-2-fluorophenyl)-7-methoxy-6-({1-[(5-methylisoxazol-3-yl)carbonyl]piperidin-4-yl}oxy)quinazolin-4-amine;

(5) *N*-(3-chloro-2-fluorophenyl)-7-methoxy-6-({1-[(5-methylisoxazol-4-yl)carbonyl]piperidin-4-yl}oxy)quinazolin-4-amine;

(6) *N*-(3-chloro-2-fluorophenyl)-7-methoxy-6-({1-[(3-methylisoxazol-4-yl)carbonyl]piperidin-4-yl}oxy)quinazolin-4-amine;

(7) *N*-(3-chloro-2-fluorophenyl)-6-({1-[(3,5-dimethylisoxazol-4-yl)carbonyl]piperidin-4-yl}oxy)-7-methoxyquinazolin-4-amine;

(8) *N*-(3-chloro-2-fluorophenyl)-7-methoxy-6-{[1-(pyridin-3-ylcarbonyl)piperidin-4-yl]oxy}quinazolin-4-amine;

(9) *N*-(3-chloro-2-fluorophenyl)-7-methoxy-6-{[1-(pyridin-2-ylcarbonyl)piperidin-4-yl]oxy}quinazolin-4-amine;

(10) *N*-(3-chloro-2-fluorophenyl)-6-{[1-(2-furoyl)piperidin-4-yl]oxy}-7-methoxyquinazolin-4-amine;

(11) *N*-(3-chloro-2-fluorophenyl)-7-{[1-(isoxazol-5-ylcarbonyl)piperidin-4-yl]oxy}-6-methoxyquinazolin-4-amine;

(12) *N*-(3-chloro-2-fluorophenyl)-6-methoxy-7-({1-[(3-methylisoxazol-5-yl)acetyl]piperidin-4-yl}oxy)quinazolin-4-amine;

(13) *N*-(3-chloro-2-fluorophenyl)-7-{[1-(pyridin-3-ylcarbonyl)piperidin-4-yl]oxy}-6-methoxyquinazolin-4-amine;

(14) *N*-(3-chloro-2-fluorophenyl)-7-{[1-(2-furoyl)piperidin-4-yl]oxy}-6-methoxyquinazolin-4-amine;

(15) *N*-(3-chloro-2-fluorophenyl)-7-methoxy-6-{[(3*R*)-1-(2-thienylacetyl)piperidin-3-yl]oxy}quinazolin-4-amine;

(16) *N*-(3-chloro-2-fluorophenyl)-6-{[(3*R*)-1-isonicotinoylpiperidin-3-yl]oxy}-7-methoxyquinazolin-4-amine;

(17) 6-({(3*R*)-1-[(2-aminopyridin-3-yl)carbonyl]piperidin-3-yl}oxy)-*N*-(3-chloro-2-fluorophenyl)-7-methoxyquinazolin-4-amine;

(18) *N*-(3-chloro-2-fluorophenyl)-7-methoxy-6-{[(3*R*)-1-(1*H*-pyrrol-2-ylcarbonyl)piperidin-3-yl]oxy}quinazolin-4-amine;

(19) *N*-(3-chloro-2-fluorophenyl)-7-methoxy-6-{[(3*R*)-1-(2-thienylcarbonyl)piperidin-3-yl]oxy}quinazolin-4-amine;

(20) *N*-(3-chloro-2-fluorophenyl)-6-{[(3*R*)-1-(2-furoyl)piperidin-3-yl]oxy}-7-methoxyquinazolin-4-amine;

(21) *N*-(3-chloro-2-fluorophenyl)-6-{[(3*R*)-1-(3-furoyl)piperidin-3-yl]oxy}-7-methoxyquinazolin-4-amine;

(22) *N*-(3-chloro-2-fluorophenyl)-7-methoxy-6-{[(3*R*)-1-(3-thienylcarbonyl)piperidin-3-yl]oxy}quinazolin-4-amine;

(23) *N*-(3-chloro-2-fluorophenyl)-7-methoxy-6-{[(3*R*)-1-(3-thienylacetyl)piperidin-3-yl]oxy}quinazolin-4-amine;

(24) *N*-(3-chloro-2-fluorophenyl)-7-methoxy-6-({(3*R*)-1-[(1-methyl-1*H*-pyrrol-2-yl)carbonyl]piperidin-3-yl}oxy)quinazolin-4-amine;

(25) *N*-(3-chloro-2-fluorophenyl)-7-methoxy-6-({(3*R*)-1-[(4-nitro-1*H*-pyrazol-1-yl)acetyl]piperidin-3-yl}oxy)quinazolin-4-amine;

(26) *N*-(3-chloro-2-fluorophenyl)-7-methoxy-6-({(3*R*)-1-[(3-methylisoxazol-5-yl)acetyl]piperidin-3-yl}oxy)quinazolin-4-amine;

(27) *N*-(3-chloro-2-fluorophenyl)-7-methoxy-6-{[(3*R*)-1-(4-{*N*,*N*-dimethylcarbamoyl}-1*H*-pyrazol-1-ylacetyl)piperidin-3-yl]oxy}quinazolin-4-amine;

(28) *N*-(3-chloro-2-fluorophenyl)-7-methoxy-6-{[(3*R*)-1-(4-cyano-1*H*-pyrazol-1-ylacetyl)piperidin-3-yl]oxy}quinazolin-4-amine;

(29) 4-({4-[(3-Chloro-2-fluorophenyl)amino]-7-methoxyquinazolin-6-yl}oxy)-*N*-phenylpiperidine-1-carboxamide;

(30) *N*-Benzyl-4-({4-[(3-chloro-2-fluorophenyl)amino]-7-methoxyquinazolin-6-yl}oxy)piperidine-1-carboxamide;

(31) 4-({4-[(3-Chloro-2-fluorophenyl)amino]-7-methoxyquinazolin-6-yl}oxy)-*N*-[4-(dimethylamino)phenyl]piperidine-1-carboxamide;

(32) 4-({4-[(3-Chloro-2-fluorophenyl)amino]-7-methoxyquinazolin-6-yl}oxy)-*N*-(2-phenylethyl)piperidine-1-carboxamide;

(33) 4-({4-[(3-Chloro-2-fluorophenyl)amino]-7-methoxyquinazolin-6-yl}oxy)-*N*-(3,4-dimethoxyphenyl)piperidine-1-carboxamide;

(34) 4-({4-[(3-Chloro-2-fluorophenyl)amino]-7-methoxyquinazolin-6-yl}oxy)-*N*-(3-fluorophenyl)piperidine-1-carboxamide;

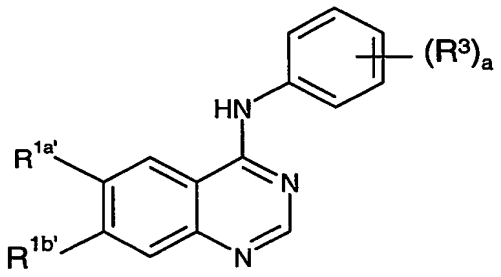
(35) 4-({4-[(3-Chloro-2-fluorophenyl)amino]-7-methoxyquinazolin-6-yl}oxy)-*N*-(3,5-dimethylisoxazol-4-yl)piperidine-1-carboxamide;

(36) 4-({4-[(3-Chloro-2-fluorophenyl)amino]-7-methoxyquinazolin-6-yl}oxy)-*N*-2-thienylpiperidine-1-carboxamide;

(37) 4-({4-[(3-chloro-2-fluorophenyl)amino]-7-methoxyquinazolin-6-yl}oxy)-*N*-3-thienylpiperidine-1-carboxamide.

32. A process for the preparation of a quinazoline derivative of the Formula I as defined in any one of the preceding claims, which process comprises either

Process (a) reacting a compound of the Formula II:



Formula II

wherein R^3 and a are as defined in claim 1 and one of $R^{1a'}$ or $R^{1b'}$ is hydroxy and the other is a group R^1 as defined in claim 1 in relation to formula (I), except that any functional group is protected if necessary,

with a compound of the Formula III:

$$Q^2\text{-}X^1\text{-}Z\text{-}Q^1\text{-}X^2\text{-}Lg$$

Formula III

wherein Q^1, Q^2, Z, X^2 and X^1 have any of the meanings defined in claim 1, except that any functional group is protected if necessary and Lg is a displaceable group:

Process (b) modifying a substituent in or introducing a substituent into another quinazoline derivative of Formula I or a pharmaceutically acceptable salt thereof as defined in claim 1, except that any functional group is protected if necessary;

Process (c) reacting a compound of the Formula II as defined in respect of process (a) above with a compound of the Formula III as defined in process (a) except Lg is OH under Mitsunobu conditions,

Process (d) for the preparation of those compounds of the Formula I wherein the group R^1

is a hydroxy group by the cleavage of a quinazoline derivative of the Formula I wherein R^1 is a (1-6C)alkoxy group;

Process (e) for the preparation of those compounds of the Formula I wherein R^1 is a (1-6C)alkoxy, (2-6C)alkenyloxy, (2-6C)alkynyloxy, or a group of the formula :

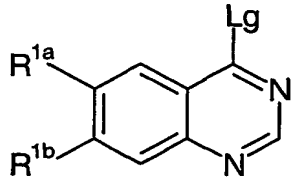
$$Q^4\text{-}X^3\text{-}$$

wherein X^3 is O and Q^4 is as defined in claim 5, by the reaction of a compound of the Formula I wherein R^1 is OH, except that any functional group is protected if necessary, with a compound of the formula $R^{1'}$-Lg, wherein $R^{1'}$ is a (1-6C)alkyl, (2-6C)alkenyl, (2-6C)alkynyl, or a group Q^4 where Q^4 is as defined in claim 5, and Lg is a displaceable group;

Process (f) for the preparation of those compounds of the Formula I wherein Q^1, Q^2 contains or R^1 is or contains a (1-6C)alkoxy or substituted (1-6C)alkoxy group or a (1-6C)alkylamino or substituted (1-6C)alkylamino group, the alkylation of a quinazoline derivative of the Formula I wherein Q^1, Q^2 contains or R^1 is or contains a hydroxy group or a primary or secondary amino group as appropriate;

Process (g) for the preparation of those compounds of the Formula I wherein R^1 is substituted by a group T, wherein T is selected from (1-6C)alkylamino, di-[(1-6C)alkyl]amino, (2-6C)alkanoylamino, (1-6C)alkylthio, (1-6C)alkylsulfinyl and (1-6C)alkylsulfonyl, the reaction of a compound which is of formula (I) except that the group R^1 is replaced with a group $R^{1''}$-Lg wherein Lg is a displaceable group, and $R^{1''}$ is a group R^1 except that it has Lg in place of the group T , and further that any functional group is protected if necessary, with a compound of the formula TH, wherein T is as defined above except that any functional group is protected if necessary;

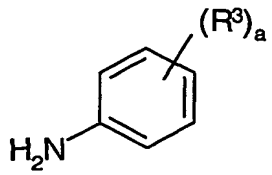
Process (h) by reacting a compound of the formula VI:



formula VI

wherein R^{1a} and R^{1b} have any of the meanings defined in claim 1 except that any functional group is protected if necessary and Lg is a displaceable group,

with an aniline of the formula VII:



formula VII

wherein R^3 and a have any of the meanings defined in claim 1, except that any functional group is protected if necessary, and wherein the reaction is conveniently performed in the presence of a suitable acid, or

Process (i) for the preparation of those compounds of the Formula I wherein Q^1 is a nitrogen containing heterocyclyl group linked to the group Z by a ring nitrogen, the coupling of a compound of the Formula I as defined in claim 1, except that the group of sub-formula (i) is a group of sub-formula (x) H-Q^1-X^2-O-, and any functional group is protected if necessary, with a compound of formula Q^2-X^1-Z-Lg, wherein Z, Q^2 and X^1 are as defined in claim 1 and Lg is a leaving group;

Process (j) for the preparation of those compounds of the Formula I define in claim 1 wherein Q^1 is a nitrogen containing heterocyclyl group linked to the -Z- group by a ring nitrogen, and Z is a group of formula –NR^{10}-C(O)-; said process comprising the coupling of a compound of the Formula I, except that the group of sub-formula (i) is a group of sub-formula (x) H-Q^1-X^2-O-, and any functional group is protected if necessary, with a compound of formula Q^2-X^1-N=C=O, wherein Q^2 and X^1 are as defined in claim 1;

and whereafter any protecting group that is present is removed by conventional means.

33. A process according to claim 32, wherein Lg is a leaving group selected from hydroxyl, chloro or bromo.

34. A pharmaceutical composition which comprises a quinazoline derivative of the Formula I, or a pharmaceutically-acceptable salt thereof, as defined in any one of claims 1 to 31 in association with a pharmaceutically-acceptable diluent or carrier.

35. A quinazoline derivative of the Formula I as defined in any one of claims 1 to 31, or a pharmaceutically acceptable salt thereof, for use as a medicament.

36. The use of a quinazoline derivative of the Formula I, or a pharmaceutically-acceptable salt thereof, as defined in any one of claims 1 to 31 in the manufacture of a medicament for use in the production of an anti-proliferative effect in a warm-blooded animal.

37. A method for producing an anti-proliferative effect in a warm-blooded animal in need of such treatment which comprises administering to said animal a quinazoline derivative of the Formula I, or a pharmaceutically acceptable salt thereof, as defined in any one of claims 1 to 31.

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